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KW

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/350,327	07/09/99	RANDOLPH	47-55

HM12/1122
GREENLEE WINNER AND SULLIVAN PC
5370 MANHATTAN CIRCLE SUITE 201
BOULDER CO 80303

EXAMINER
GUTTMAN, H

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/22/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)
	09/350,327	RANDOLPH ET AL.
	Examiner	Art Unit
	Harry J Guttman	1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) 11-20 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-10 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) <input type="checkbox"/> Notice of References Cited (PTO-892)	18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
17) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4, 5</u> .	20) <input type="checkbox"/> Other: _____

DETAILED ACTION

Election/Restrictions

Claims 11-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 7.

As such, Claims 1-10 are examined on their merits.

Claim Objections

Claim 10 is objected to because of the following informalities: An “and” is missing between the last two items in the Markush Group. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the use of the phrase in step (b) "adding to the mixture a chaotropic agent at a concentration of from 0M..." is improper. To add something at zero concentration is an oxymoron. It is suggested that a phrase such as "up to about 8 M", be used in place of the current concentration range specified.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention as described on page 6 makes use of a two-step pressure treatment of an aggregated protein mixture. However, the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use this method commensurate in the scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (a) the breadth of the claims; (b) the nature of the invention; (c) the state of the prior art; (d) the level of one of ordinary skill; (e) the level of predictability in the art; (f) the amount of direction provided by the inventor; (g) the existence of working

examples; and (h) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. While all of these factors are considered, a sufficient number are discussed below so as to create a *prima facie* case.

The breadth of the claims reads on a procedure that can be used on any aggregated protein mixture to produce active protein of any type (e.g. monomeric, oligomeric, membrane bound, membrane associated, filament-forming etc...). It is well known in the art that most proteins, if denatured or aggregated in an inclusion body, do not readily renature using a single method of treatment. Some proteins, if denatured or aggregated in an inclusion body, have no treatment that can be used to yield active protein (e.g., insulin and other multimeric proteins). Further, it is also well known in the art that the native, active form of a protein is typically not the lowest energy configuration; in producing the protein the cell is actively involved in creating its configuration. Thus, while it may be possible that the procedure, as described in the claims, could be useful for a limited number of monomeric proteins, it seems highly unlikely that this procedure could be used for all types of proteins even after extensive experimentation.

There is no guidance from the application as to what extent the pressure should be applied in the first step for which protein (or type thereof), nor to what extent the pressure should be decreased in the second step for a given protein (or type thereof). Similarly, there is no guidance given to the temperature, or range thereof, that would be reasonable to try or use. Given that temperature and pressure are critical to both the thermodynamics and kinetics of protein aggregation and renaturation, it seems both

should be discussed and specified so as to give direction of how they should be chosen for a proper working embodiment of the invention. Thus given high level of unpredictability in the art, as described above, one of ordinary skill in the art at the time of the invention would require a substantial inventive contribution to practice the invention, especially with its current breadth.

Finally, applicant presents no working embodiment of the two-step pressure disaggregation process. Example 4 discloses only one pressure step, and does not present protein activity measurements or soluble protein determination so that the effectiveness of the procedure can be assessed. Example 5 teaches no pressure step, no activity measurements, and no determination of the soluble protein concentration; this example shows no embodiment of the invention. Example 6 teaches only one pressure step, yet teaches against the preferred embodiment (of using guanidine hydrochloride) since increasing the guanidine hydrochloride concentration show a decreasing trend in β -lactamase activity. Since examples 1-3 do not teach the invention, there appears to be no working embodiment of the invention. While the absence of a working embodiment can not be a sole factor in determining enablement, its absence, in light of the unpredictable nature of the art and the lack of direction provided by the applicant presents, provides additional weight to the lack of enablement in consideration of the Wands factors as a whole. Thus, one of ordinary skill in the art would not have a reasonable expectation of success in using the claimed invention.

No claims are allowed.

Any inquiry concerning this communication should be directed to Harry J. Guttman, Ph.D. at telephone number (703) 305-0159. The examiner can normally be reached during the hours of 08:00 to 16:30 Eastern Time.

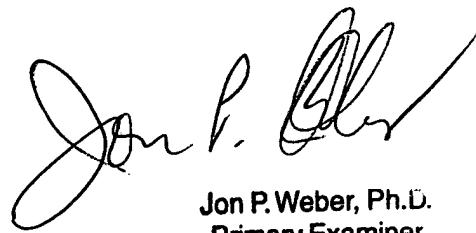
If attempts to reach the examiner by telephone are unsuccessful, a message may be left on the voice mail. The fax number for Art Unit 1651 is (703) 308-4242 or 305-3014. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. My supervisor, Michael Wityshyn, may be contacted at (703) 308-4743.

All internet e-mail communications will be made of record in the application file. PTO employees will not communicate with applicant via internet e-mail where sensitive data will be exchanged or where there exists a possibility that sensitive data could be identified or exchanged unless there is of record an express waiver of the confidentiality requirements of 35 U.S.C. 122 by the applicant. See the Interim Internet Usage Policy published in the Patent and Trademark Office Official Gazette on 25 February 1997 at 1195 OG 89.

H.J.G. 20 November 2000



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Jon P. Weber, Ph.D.
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